

In re Appln. of Burke, Jr., et al.  
Application No. 09/937,150

### REMARKS

#### Discussion of Claim Amendments

The claims have been amended to expedite the prosecution. Claims 39 and 40 have been amended to include a description of the various parts of the phenylalanyl radical of Y such that a reference has been made to the  $-\text{CH}_2\text{CH}<$  group. This makes it further clear that the substituents of the phenyl ring can be present in one of the remaining 5 positions (not the position attached to the  $-\text{CH}_2\text{CH}<$  group). In addition, the "keto" substituent has been deleted from the list of further substituents of the alkyl portion of the substituents of the phenyl ring. As regards the term "the substituents" referring to the aryl and alkyl portions of W, the term has been replaced with "W". Carboxyl and amino have been deleted from the list of substituents of aryl and alkyl portions of W. It has been expressly recited that Z can be substituted or unsubstituted. Aryl is expressly recited as carbocyclic aryl. The proviso has been amended to exclude arylalkylamino as Z when carboxyalkyloxy is a substituent of the phenyl ring and W is oxalyl or acetyl.

A new proviso has been added to claim 39 to exclude arylalkylamino (as Z) when W is arylalkoxycarbonyl and the substituent on the phenyl ring is phosphonomethyl. A new proviso has been added to claim 40 to exclude arylalkylamino (as Z) when W is aryl methoxycarbonyl and the substituent on the phenyl ring is phosphonomethyl.

Claim 41 has been rewritten as independent claim. Claim 47 has been amended to remove  $\text{R}_4$  since formula XII does not have  $\text{R}_4$ . Claims 49 and 116 have been amended to replace the term "the substituents" with "--W--". Claim 73 has been amended to exclude a situation where F and G are simultaneously C.

Claim 116 has been amended to further describe the phenylalanyl radical. In addition, the substituent "dicarboxyhalo  $\text{C}_1\text{-C}_6$  alkyl" has been deleted from the substituents on the phenyl ring. Aryl has been defined as a carbocyclic aryl. Claims 117 and 121 have been amended to recite that the composition is a pharmaceutical composition to further sharpen the claim language. Claim 123 has been amended to direct it to a method of inhibiting proliferation of cells. Claim 124 has been amended to include the term "in need thereof" to further sharpen the claim language. Claim 133 has been amended to direct it to breast cancer

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treatment. Claim 136 has been amended to recite specific cancer treatments. New claims 140-158 have been added and are directed to embodiments of the invention.

No new matter has been added.

### The Present Invention

With the entry of the amendment, claims 39-49, 67-68, 73, 78, 85, 116-117, 120-124, 126-130, 133, 136, and 140-158 would be pending.

### The Office Action

The Office Action sets forth the following grounds for rejection: (1) claims 123-124 are rejected under 35 USC § 101, for an alleged lack of utility; (2) claims 39-40 and 116 are rejected under the doctrine of obviousness-type double patenting as allegedly unpatentable over claim 1, 10, or 11 of Burke (USP 6,307,090); (3) claims 123, 133, and 136 rejected under 35 U.S.C. § 112, first paragraph, for an alleged non-enablement; (4) claims 39-49, 67, 68, 73, 78, 85, 116, 117, 120-124, 126-130, 133, 136, and 139 are rejected under 35 U.S.C. § 112, second paragraph, for an alleged indefiniteness; (5) claims 39, 40, 49, 72, 78, and 85 are rejected under 35 U.S.C. § 102(a), as allegedly anticipated by Al-Obeidi (USP 5,849,510); (6) claims 39-40 and 116 are rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Burke; (7) claims 39-40 are rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Hiyoshi (USP 5,824,862); Harding (USP 6,022,696); Landry (USP 5,948,658); Dimaio (WO 98/50241); or Lunney (USP 5,922,697); and (8) claims 39-40 are rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Lunney.

### Discussion of Rejections

#### *1. Utility*

Although applicants disagree with the rejection, applicants have amended claims 123 and 124. In view of the foregoing, the present claims meet the utility requirement. Accordingly, the rejection should be withdrawn.

#### *2. Obviousness-Type Double Patenting*

As claims 39-40 have been amended, applicants believe that there is no obviousness-type double patenting over claim 1, 10 or 11 of Burke. Note in claims 39-40, the proviso

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excludes arylalkylamino when W is oxalyl or acetyl and the phenyl ring contains carboxyalkyloxy at the *para* position. In claim 116, the list of substituents for phenyl has been amended to remove dicarboxyhalo C<sub>1</sub>-C<sub>6</sub> alkyl. In addition, halo has been removed from the list of further substituents. Claims 1, 10 and 11 of Burke do not suggest to those of ordinary skill in the art the subject matter of the present claims.

In view of the foregoing, the obviousness-type double patenting rejection should be removed.

### *3. Non-Enablement*

The Office Action has rejected claims 123, 133, and 136 as allegedly lacking enablement. Claim 123 has been amended as discussed. Claim 133 has been amended to direct the method to breast cancer treatment. Applicants show that a compound of the invention inhibits the growth of MDA-MB 453/M1 human breast cancer xenograft. Claim 136 has been amended to recite specific cancer treatments, the efficacy of which the present claimed compounds can enhance. Applicants teach those skilled in the art how to practice the claimed invention. Accordingly, the non-enablement rejection should be withdrawn.

### *4. Indefiniteness*

The Office Action alleges that claims 39-49, 67, 68, 73, 78, 85, 116, 120-124, 126-130, 133, 136, and 139 are indefinite. Applicants have amended claims 39-40, 73, and 116. Claim 41 has been rewritten as independent claim. The rejection of claim 120, applicants respectfully submit, is erroneous. The compound of claim 120 contains a malonyl group at the *para* position. Please note that a compound where Z is arylalkylamino having malonyl on the phenyl at the *para* position has not been excluded (see proviso in claim 39). Accordingly, claim 120 is properly dependent upon claim 39. Claim 123 has been amended to improve grammar. Further, the term "preventing" does not appear in amended claim 123. The amended claims meet the statutory requirement. Claims 41-49, 67, 68, 73, 78, 85, 117, 122, 124, 133, 136, and 139 are dependent claims. Accordingly, the indefiniteness rejection should be withdrawn. Claims 140-158 also should not be rejected on this basis.

### *5. Anticipation or obviousness*

Claims 39, 40, 49, 72, 78, and 85 stand rejected as allegedly anticipated by Al-Obeidi. Claims 39 and 40 have been amended to further clarify that aryl is carbocyclic aryl. Claims

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49, 78, and 85 are dependent claims. Claim 72 remains canceled. Accordingly, Al-Obeidi fails to anticipate the present claims.

Claims 39, 40, and 116 stand rejected as allegedly anticipated by Burke. Applicants have amended claims 39 and 40 to exclude arylalkylamino when W is acetyl and the phenyl ring contains certain substituents. The rejection of claim 116, applicants respectfully submit, is erroneous. The specific selection of substituents recited for the phenyl ring (in the paragraph relating to Y) does not encompass the compounds disclosed in scheme 3 at column 29 of Burke. For example, according to selection (ii) both hydroxyl and carboxy C<sub>1</sub>-C<sub>6</sub> alkyl must be present. Burke discloses, in contrast, a compound having only hydroxyl (compound 18a). If the alkyl portion of any of the recited substituents or combinations of substituents are further substituted with a listed further substituent, the resulting compounds do not read on Burke's scheme 3 compounds. Accordingly, claims 39, 40, and 116 should not be rejected over Burke.

Claims 39-40 stand rejected as allegedly anticipated by Hiyoshi, Harding, or Landry. Applicants have amended these claims to remove carboxyl and amino from the list of substituents on the alkyl and aryl portions of W. The amended claims do not read on Hiyoshi, Harding, or Landry. Accordingly, the rejections should be removed.

Claims 39-40 stand rejected as allegedly anticipated by Dimaio. Applicants respectfully disagree. The Office Action does not clearly identify the compound alleged to anticipate the claims. Assuming the compound on the right hand side of the reaction shown in lines 11-14 at page 35 is the compound the Office Action is referring to, this compound contains a phenyl ring having two methyl groups at the two ortho positions of the phenyl ring. Such a compound is not within the scope of the claimed invention. In view of the foregoing, the anticipation rejection over Dimaio should be removed.

Claims 39-40 stand rejected as allegedly anticipated or rendered obvious by Lunney. Applicants have amended claim 41 to make it independent of claim 40. The Office Action's interpretation has been rendered inapplicable. The hydrogen atom of the hydroxyl group cannot be replaced by any group. The compounds encompassed by the claims are clearly set forth. There is no claim interpretation issue here. Claims 39-40 do not encompass phosphate as the Office Action contends.

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Further, the present claims do not cover the precursors of the compound disclosed at col. 28, lines 27-45 or the compound disclosed in example 19 of Lunney. Claims 39-40 do not encompass compounds wherein Z is arylalkylamino when W is acetyl and the phenyl ring has a hydroxyl substituent at the para position and hydrogen at the ortho and meta positions (i.e., unsubstituted at ortho and meta positions). Accordingly, the anticipation and obviousness rejections should not apply to amended claims 39-40.

New claims 140-158 also should not be rejected.

#### Conclusion

The application is considered in good and proper form for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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